**Amendments to the Specification**

Please replace the paragraph at page 8, line 17, to page 9, line 9, with the following amended paragraph:

In the present application, amino acid names and atom names (e.g. CA, CB, CD, CG, SG, NZ, N, O, C, etc) are used as defined by the Protein DataBank (PDB) ~~(www.pdb.org)~~ which are based on the IUPAC nomenclature (IUPAC Nomenclature and Symbolism for Amino Acids and Peptides (residue names, atom names etc.), *Eur. J. Biochem.*, 138, 9-37 (1984) together with their corrections in *Eur. J. Biochem.*, 152, 1 (1985). CA is sometimes referred to as Cα, CB as Cβ. The term "amino acid residue" is intended to indicate an amino acid residue contained in the group consisting of alanine (Ala or A), cysteine (Cys or C), aspartic acid (Asp or D), glutamic acid (Glu or E), phenylalanine (Phe or F), glycine (Gly or G), histidine (His or H), isoleucine (Ile or I), lysine (Lys or K), leucine (Leu or L), methionine (Met or M), asparagine (Asn or N), proline (Pro or P), glutamine (Gln or Q), arginine (Arg or R), serine (Ser or S), threonine (Thr or T), valine (Val or V), tryptophan (Trp or W), and tyrosine (Tyr or Y) residues.

Please replace the paragraph at page 12, lines 18-31 with the following amended paragraph:

The polypeptide is normally cleared by the action of one or more of the reticuloendothelial systems (RES), kidney, spleen or liver, or by specific or unspecific proteolysis. The term "renal clearance" is used in its normal meaning to indicate any clearance taking place by the kidneys, e.g. by glomerular filtration, tubular excretion or tubular elimination. Normally, renal clearance depends on physical characteristics of the polypeptide, including molecular weight, size (relative to the cutoff for glomerular filtration), symmetry, shape/rigidity, charge and attached carbohydrate chains. A molecular weight of about 67 kDa is normally considered to be a cut-off-value for renal clearance. Renal clearance may be measured by any suitable assay, e.g. an established *in vivo* assay. For instance, renal clearance may be determined by administering a labelled (e.g. radiolabelled or fluorescence labelled) conjugated polypeptide to a patient and measuring the label activity in urine collected from the patient. Reduced renal clearance is determined relative to the reference molecule, such as glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimmune®~~ <u>ACTIMMUNE®</u>

interferon gamma. The functionality to be retained is normally selected from antiviral, antiproliferative or immunomodulatory activity.

Please replace the paragraph at page 13, line 24 to page 14, line 10 with the following amended paragraph:

The term "exhibiting IFNG activity" is intended to indicate that the variant has one or more of the functions of native glycosylated huIFNG or ~~Actimmune®~~ ACTIMMUNE® interferon gamma, including the capability to bind to an IFNG receptor and cause transduction of the signal transduced upon huIFNG-binding of its receptor as determined *in vitro* or *in vivo* (i.e. *in vitro* or *in vivo* bioactivity). The IFNG receptor has been described by Aguet et al. (Cell 55:273-280, 1988) and Calderon et al. (Proc. Natl. Acad. Sci. USA 85:4837-4841, 1988). A suitable assay for testing IFNG activity is the assay entitled "Primary Assay" disclosed herein. When using the "Primary Assay" described herein, polypeptide variants "exhibiting IFNG activity" have a specific activity of at least 5% as compared to glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimmune®~~ ACTIMMUNE® interferon gamma. It will be understood that depending on which specific modifications are performed, for example whether the variant is PEGylated or not, this may lead to activities over a wide range. Thus, examples of specific activities may range from as low as 5% to as high as 150% as compared to glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimmune®~~ ACTIMMUNE® interferon gamma. For example, the specific activity may be at least 10% (e.g. 10-125%), such as at least 15% (e.g. 15-125%), e.g. at least 20% (such as 20-125%), at least 25% (e.g. 25-125%), at least 30% (e.g. 30-125%), at least 35% (e.g. 35-125%), at least 40% (e.g. 40-125%), at least 45% (e.g. 45-125%), at least 50% (e.g. 50-125%), at least 55% (e.g. 55-125%), at least 60% (e.g. 60-125%), at least 65% (e.g. 65-125%), at least 70% (e.g. 70-125%), at least 75% (e.g. 75-125%), at least 80% (e.g. 80-125%) or at least 90% (e.g. 90-110%) as compared to the specific activity of glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimmune®~~ ACTIMMUNE® interferon gamma.

Please replace the paragraph at page 14, lines 11-17 with the following amended paragraph:

It may be beneficial that the variant has a decreased receptor-binding affinity and hence a decreased IFNG activity as compared to glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimmune®~~ ACTIMMUNE® interferon gamma in order to decrease receptor-mediated clearence. For example, the variant may exhibit 1-75% (e.g. 5-75%), such as 1-50% (e.g. 5-50%), e.g. 1-40% (e.g. 5-40%), 1-30% (e.g. 5-30%), 1-20% (e.g. 5-20%) or 1-10% (e.g. 5-10%) of the IFNG activity of glycosylated huIFNG, glycosylated [S99T]huIFNG or ~~Actimunne®~~ ACTIMMUNE® interferon gamma when tested in the "Primary Assay" described herein.

Please replace the paragraph at page 16, lines 1-4 with the following amended paragraph:

When used herein the term "~~Actimmune®~~ ACTIMMUNE®" refers to the 140 amino acid form of IFNG (disclosed in SEQ ID NO:3) achieved by fermentation of a genetically engineered *E.coli* bacterium. ~~Actimmune®~~ ACTIMMUNE® interferon gamma is un-glycosylated. ~~Further information of Actimmune® is available on www.actimmune.com.~~

Please replace the paragraph at page 63, lines 5-10 with the following amended paragraph:

Non-ionic surfactants or detergents (also known as "wetting agents") may be present to help solubilize the therapeutic agent as well as to protect the therapeutic polypeptide against agitation-induced aggregation, which also permits the formulation to be exposed to shear surface stress without causing denaturation of the polypeptide. Suitable non-ionic surfactants include polysorbates (20, 80, etc.), polyoxamers (184, 188 etc.), ~~Pluronic®~~ PLURONIC® polyols, polyoxyethylene sorbitan monoethers (~~Tween®~~ TWEEN®-20 polysorbate surfactant, ~~Tween®~~ TWEEN®-80 polysorbate surfactant, etc.).

Please replace the paragraph at page 65, lines 10-12 with the following amended paragraph:

The presently preferred sulfoalkyl ether cyclodextrin derivative is a salt of beta cyclodextrin sulfobutyl ether (in particular the sodium salt thereof also termed SBE7-β-CD which is available as ~~Captisol®~~ CAPTISOL® cyclodextrin) (Cydex, Overland Park, Kansas 66213, US).

Please replace the paragraph at page 65, line 15 to page 66, line 1 with the following amended paragraph:

Suitable examples of sustained-release preparations include semi-permeable matrices of solid hydrophobic polymers containing the variant, the matrices having a suitable form such as a film or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate) or poly(vinylalcohol)), polylactides, copolymers of L-glutamic acid and ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the ~~ProLease®~~ PROLEASE® technology or ~~Lupron Depot®~~ LUPRON DEPOT® (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for long periods such as up to or over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated polypeptides remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.